

=> d his

(FILE 'HOME' ENTERED AT 15:14:42 ON 06 SEP 2006)

L1 FILE 'REGISTRY' ENTERED AT 15:14:54 ON 06 SEP 2006
L2 STRUCTURE UPLOADED
0 S L1 SSS SAM

FILE 'HOME' ENTERED AT 15:15:38 ON 06 SEP 2006

L3 FILE 'REGISTRY' ENTERED AT 15:16:57 ON 06 SEP 2006
L4 STRUCTURE UPLOADED
L5 0 S L3 SSS SAM
10 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:17:46 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 15:18:00 ON 06 SEP 2006

FILE 'CAPLUS' ENTERED AT 15:18:07 ON 06 SEP 2006

L6 FILE 'HCAPLUS' ENTERED AT 15:18:44 ON 06 SEP 2006
9 S L5

FILE 'HOME' ENTERED AT 15:20:12 ON 06 SEP 2006

L7 FILE 'REGISTRY' ENTERED AT 15:29:57 ON 06 SEP 2006
1 S 375371-24-7/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'HOME' ENTERED AT 15:30:14 ON 06 SEP 2006

FILE 'HCAPLUS' ENTERED AT 15:36:51 ON 06 SEP 2006

FILE 'HOME' ENTERED AT 15:37:07 ON 06 SEP 2006

L8 FILE 'REGISTRY' ENTERED AT 16:23:30 ON 06 SEP 2006
L9 STRUCTURE UPLOADED
L10 0 S L8 SSS SAM
2 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:24:34 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 16:24:53 ON 06 SEP 2006

L11 FILE 'HCAPLUS' ENTERED AT 16:25:00 ON 06 SEP 2006
2 S L10

FILE 'HCAPLUS' ENTERED AT 16:25:30 ON 06 SEP 2006

=> s l10

L12 2 L10

=> d ibib abs hitstr 1-2



chain nodes :

11 12 13 14 15 16 17 20 21 22 23 28

ring nodes :

1 2 3 4 5 6 7 8 9 10

chain bonds :

7-11 9-12 13-14 13-17 14-15 15-16 20-21 21-22 22-23

ring bonds :

1-2 1-6 1-10 2-3 3-4 4-5 4-10 5-6 5-7 6-9 7-8 8-9

exact/norm bonds :

1-2 1-6 1-10 2-3 3-4 4-5 4-10 5-6 5-7 6-9 7-8 7-11 8-9 9-12 13-14 13-17 14-15
15-16 20-21 21-22 22-23

G1:A,Cb,Cy,Hy,Id,Ak,C,P,Si,B

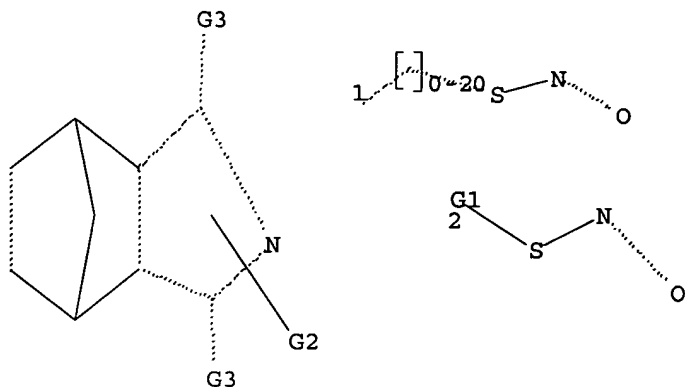
G2:[*1],[*2]

G3:O,S

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 20:CLASS 21:CLASS 22:CLASS
23:CLASS 28:CLASS 29:CLASS

=> d l8
 L8 HAS NO ANSWERS
 L8 STR



G1 A,Cb,Cy,Hy,Id,Ak,C,P,Si,B

G2 [@1],[@2]

G3 O,S

Structure attributes must be viewed using STN Express query preparation.

=> s l8 sss sam
 SAMPLE SEARCH INITIATED 16:24:12 FILE 'REGISTRY'
 SAMPLE SCREEN SEARCH COMPLETED - 560 TO ITERATE

100.0% PROCESSED 560 ITERATIONS 0 ANSWERS
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
 PROJECTED ITERATIONS: 9781 TO 12619
 PROJECTED ANSWERS: 0 TO 0

L9 0 SEA SSS SAM L8

=> s l8 sss full
 FULL SEARCH INITIATED 16:24:27 FILE 'REGISTRY'
 FULL SCREEN SEARCH COMPLETED - 10896 TO ITERATE

100.0% PROCESSED 10896 ITERATIONS 2 ANSWERS
 SEARCH TIME: 00.00.01

L10 2 SEA SSS FUL L8

| | | |
|--|------------|---------|
| => fil hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 167.38 | 406.11 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -6.75 |

FILE 'HCAPLUS' ENTERED AT 16:24:34 ON 06 SEP 2006
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Sep 2006 VOL 145 ISS 11
FILE LAST UPDATED: 5 Sep 2006 (20060905/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

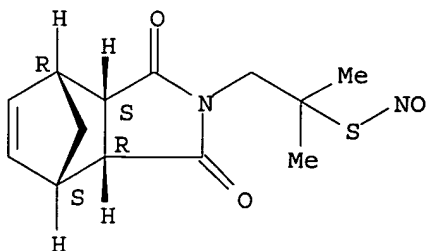
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d scan

YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

L10 2 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Thionitrous acid (HNOS), S-[2-[(3aR,4S,7R,7aS)-1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl]-1,1-dimethylethyl] ester, rel- (9CI)
MF C13 H16 N2 O3 S

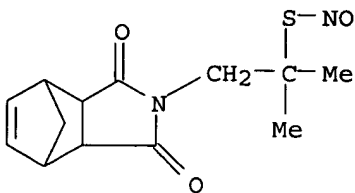
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L10 2 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Thionitrous acid (HNOS), S-[2-(1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl)-1,1-dimethylethyl] ester, rel- (9CI)
MF C13 H16 N2 O3 S



.
=>
=>
=>
=>
=>
=>
=>

| | | |
|--|------------|---------|
| => fil hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 2.53 | 411.61 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -6.75 |

FILE 'HCAPLUS' ENTERED AT 16:25:30 ON 06 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 6 Sep 2006 VOL 145 ISS 11
FILE LAST UPDATED: 5 Sep 2006 (20060905/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 15:14:42 ON 06 SEP 2006)

FILE 'REGISTRY' ENTERED AT 15:14:54 ON 06 SEP 2006

L1 STRUCTURE UPLOADED
L2 0 S L1 SSS SAM

FILE 'HOME' ENTERED AT 15:15:38 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 15:16:57 ON 06 SEP 2006

L3 STRUCTURE UPLOADED
L4 0 S L3 SSS SAM
L5 10 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:17:46 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 15:18:00 ON 06 SEP 2006

FILE 'CAPLUS' ENTERED AT 15:18:07 ON 06 SEP 2006

FILE 'HCAPLUS' ENTERED AT 15:18:44 ON 06 SEP 2006
L6 9 S L5

FILE 'HOME' ENTERED AT 15:20:12 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 15:29:57 ON 06 SEP 2006
L7 1 S 375371-24-7/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'HOME' ENTERED AT 15:30:14 ON 06 SEP 2006

FILE 'HCAPLUS' ENTERED AT 15:36:51 ON 06 SEP 2006

FILE 'HOME' ENTERED AT 15:37:07 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 16:23:30 ON 06 SEP 2006
L8 STRUCTURE UPLOADED
L9 0 S L8 SSS SAM
L10 2 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:24:34 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 16:24:53 ON 06 SEP 2006

FILE 'HCAPLUS' ENTERED AT 16:25:00 ON 06 SEP 2006
L11 2 S L10

FILE 'HCAPLUS' ENTERED AT 16:25:30 ON 06 SEP 2006

=> s l10

L12 2 L10

=> d ibib abs hitstr 1-2

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:836762 HCAPLUS

DOCUMENT NUMBER: 139:350474

TITLE: Preparation and compositions of nitrosothio
(hetero)cyclic nitric oxide donors

INVENTOR(S): Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Lin,
Chia-en; Ranatunga, Ramani R.; Richardson, Stewart K.;
Wang, Tiansheng; Wang, Weiheng; Wey, Shio-jyi

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

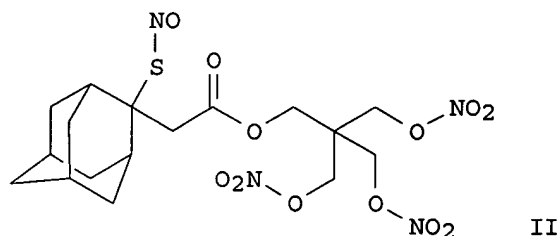
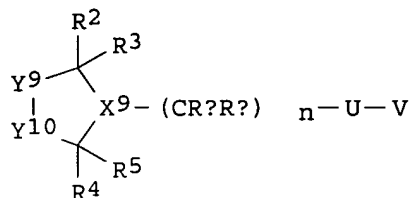
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|---|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2003086282 | A2 | 20031023 | WO 2003-US10562 | 20030407 |
| WO 2003086282 | A3 | 20040429 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | |

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2480832 AA 20031023 CA 2003-2480832 20030407
 AU 2003223491 A1 20031027 AU 2003-223491 20030407
 US 2003203915 A1 20031030 US 2003-407420 20030407
 EP 1497268 A2 20050119 EP 2003-719621 20030407
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2005537223 T2 20051208 JP 2003-583309 20030407
 PRIORITY APPLN. INFO.: US 2002-369873P P 20020405
 WO 2003-US10562 W 20030407
 OTHER SOURCE(S): MARPAT 139:350474
 GI



AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO₂; X₉ = CR₁₀ or N; Y₉ = CR₆R₇, NR_i, NR₂₅, NR_iCR₆R₇, CR₆R₇NR_i, CR₂R₃CR₆R₇, or CR₆R₇CR₂R₃; Y₁₀ = CR₈R₉ or CR₈R₉CR₁₇R₁₈; R₂-R₉, R₁₇, and R₁₈ = independently H or alkyl; or R₂R₃, R₄R₅, R₆R₇, or R₈R₉ = independently oxo; or R₄ and R₇ together with the C's to which they are attached = cycloalkyl; or CR₆R₇ = cycloalkyl; R₆ and R₉ taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R₇ and R₈ are not present; R₄ and R₂₅ taken together with the C and N to which they are attached = heterocyclyl; R_a = lone pair of electrons, H, or (aryl)alkyl; R_e and R_f = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CR_eR_f = heterocyclyl or (bridged) cycloalkyl; R_i = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH₂Cl₂ to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC₅₀ of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight

inhibition, or exhibited much higher IC50 values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

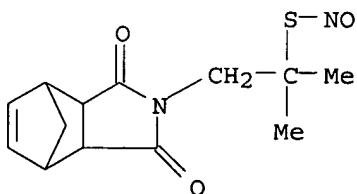
IT 618112-23-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nitric oxide donor; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

RN 618112-23-5 HCAPLUS

CN Thionitrous acid (HNO_S), S-[2-(1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl)-1,1-dimethylethyl] ester, rel- (9CI) (CA INDEX NAME)



L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:868945 HCAPLUS
DOCUMENT NUMBER: 136:575
TITLE: Infrared thermography and methods of use
INVENTOR(S): Marek, Przemyslaw A.; Trocha, Andrzej M.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2001046471 | A1 | 20011129 | US 2001-850081 | 20010508 |
| US 6762202 | B2 | 20040713 | | |
| US 2004162243 | A1 | 20040819 | US 2004-781705 | 20040220 |
| PRIORITY APPLN. INFO.: | | | US 2000-202935P | P 20000509 |
| | | | US 2001-850081 | A1 20010508 |

OTHER SOURCE(S): MARPAT 136:575

AB The present invention describes rapid noninvasive methods for measuring vasodilation or changes in blood flow in a patient following administration of at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one vasoactive agent. The method comprises the administration of at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of

endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one vasoactive agent to the patient followed by monitoring the temperature change of an area of interest using IR thermog. The present invention provides methods for diagnosing diseases or disorders related to vasodilation and changes in blood flow, such as, sexual dysfunction, Raynaud's syndrome, inflammation, hypertension, gastrointestinal disorders and central nervous system disorders. The sexual dysfunction is preferably female sexual dysfunction and female sexual arousal. The vasoactive agents include potassium channel activators, calcium channel blockers, α -adrenergic receptor antagonists, β -blockers, phosphodiesterase inhibitors, adenosine, ergot alkaloids, vasoactive intestinal peptides, prostaglandins, dopamine agonists, opioid antagonists, endothelin antagonists and thromboxane inhibitors. The present invention can also be used to screen and identify drug candidates for treating diseases, disorders and conditions resulting from vasodilation or changes in blood flow. The present invention also describes compns. comprising at least one S-nitrosothiol compound for diagnosing, monitoring and/or treating female sexual dysfunctions.

IT 375371-22-5P

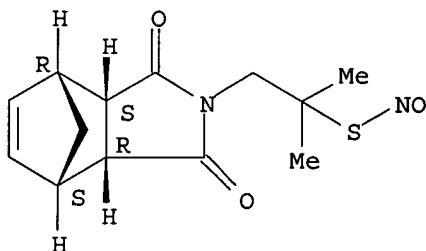
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(IR thermog. for measuring vasodilation or changes in blood flow following administration of nitric oxide donor)

RN 375371-22-5 HCAPLUS

CN Thionitrous acid (HNOS), S-[2-[(3aR,4S,7R,7aS)-1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl]-1,1-dimethylethyl] ester, rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:hold

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 15.28 | 426.89 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| -1.50 | -8.25 |

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 16:26:32 ON 06 SEP 2006

Connecting via Winsock to STN

=> d his

(FILE 'HOME' ENTERED AT 15:14:42 ON 06 SEP 2006)

FILE 'REGISTRY' ENTERED AT 15:14:54 ON 06 SEP 2006
STRUCTURE UPLOADED

L1
L2

0 S L1 SSS SAM

FILE 'HOME' ENTERED AT 15:15:38 ON 06 SEP 2006

FILE 'REGISTRY' ENTERED AT 15:16:57 ON 06 SEP 2006
STRUCTURE UPLOADED

L3
L4
L5

0 S L3 SSS SAM

10 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:17:46 ON 06 SEP 2006

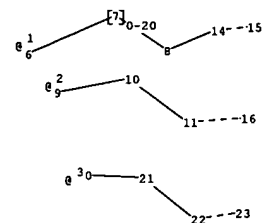
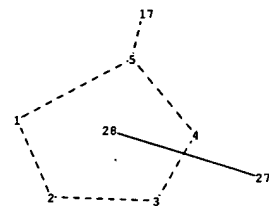
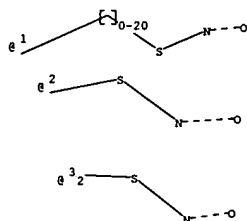
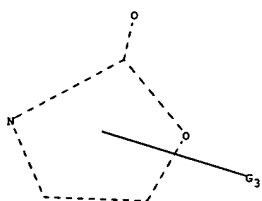
FILE 'REGISTRY' ENTERED AT 15:18:00 ON 06 SEP 2006

FILE 'CAPLUS' ENTERED AT 15:18:07 ON 06 SEP 2006

FILE 'HCAPLUS' ENTERED AT 15:18:44 ON 06 SEP 2006

L6

9 S L5



chain nodes :

6 7 8 9 10 11 14 15 16 17 20 21 22 23 27

ring nodes :

1 2 3 4 5

chain bonds :

5-17 6-7 7-8 8-14 9-10 10-11 11-16 14-15 20-21 21-22 22-23

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 5-17 7-8 8-14 9-10 10-11 11-16 14-15 20-21 21-22 22-23

exact bonds :

6-7

G2:C,P,B,M,Cb,Cy,Hy,Id,Ak

G3:[*1],[*2],[*3]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS7:CLASS8:CLASS9:CLASS10:CLASS11:CLASS14:CLASS15:CLASS16:CLASS17:CLASS20:CLASS21:CLASS22:CLASS23:CLASS27:CLASS28:CLASS